SN 10,017,643
Docket No. S-96,583

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

Claim 1 (currently amended): A method ~~for improving~~ using density modification to remove atomic model bias of an electron density map representing a crystal structure comprising:

(a) obtaining by x-ray diffraction observed structure factor amplitudes for a plurality of reflections from the crystal structure;

(b) ~~selecting a starting set of crystallographic phases to combine with the observed structure factor amplitudes to form a first set of structure factors~~ using a starting model of the crystal structure to calculate a starting set of crystallographic phases, and combining the starting set of crystallographic phases with the observed structure factor amplitudes to form a first set of structure factors;

(c) deriving an ~~first~~ electron density map from the current set of structure factors;

(d) ~~identifying~~ selecting specific features of the ~~first~~ electron density map ~~to obtain expected distributions of electron density~~ not used in the calculation of the first set of structure factors from the group consisting of: flatness of solvent region, non-crystallographic symmetry, structural motifs, probability distributions for electron density in regions containing macromolecule, and probability distributions for electron density in solvent regions; and using the specific features to construct probability functions for electron density for each point in the electron density map;

(e) evaluating the overall probability that the electron density map is correct by making a comparison between the ~~first~~ electron density map and the ~~expected distribution of electron density~~ probability functions for electron density for each point in the map;

(f) estimating how changes in the crystallographic phase of a reflection *k* affect the comparison;

(g) establishing crystallographic phase probability distributions from the comparisons for the possible crystallographic phases of reflection *k*, absent phase information from the starting model of the crystal structure;

(h) repeating steps (c) through (g) as *k* is indexed through all of the plurality of reflections;

(i) determining a set of the most probable crystallographic phases for each one of the reflections from the crystallographic phase probability distributions; and

(j) deriving an updated electron density map using the observed structure factor amplitudes and the set of crystallographic phases determined to be most probable from the crystallographic phase probability distributions for each one of the reflections;

(k) repeating steps (d) through (j) with the ~~first~~ electron density map replaced with each updated electron density map until changes in the set of crystallographic phases become minimal between successive iterations to obtain a final set of crystallographic phases with minimum bias from known electron density maps; and

(l) forming a final electron density map using the final set of crystallographic phases.

Claim 2 (currently amended): The method of Claim 1, wherein identifying features of the electron density map includes making probability estimates of whether each point in the map is located in ~~a~~ the solvent region or a ~~crystal structure~~ region containing the macromolecule.

Claim 3 (currently amended): The method of Claim 1, wherein identifying features of the ~~election~~ electron density map includes estimates of whether the electron density

at each point in the map is related by non-crystallographic symmetry to electron density at another point in the map.

Claim 4 (previously presented): The method of Claim 1, wherein identifying features of the electron density map includes estimates of whether a structural motif is located at each point in the map.

Claim 5 (original): The method of Claim 4, wherein the structural motif is a helix.

Claim 6 (canceled)

Claim 7 (currently amended): The method of Claim 1, wherein the step of determining a set of the most probable crystallographic phases further includes the steps of calculating first and second derivatives for the crystallographic phase probability distributions with respect to the structure factors; and

applying a Fast Fourier Transform-based algorithm to determine the most probable crystallographic phase probability distributions for the ~~first~~ electron density map.

Claim 8 (currently amended): The method of Claim 1, wherein the step of selecting a starting set of crystallographic phases includes;

selecting a model crystal structure having similarities to the crystal structure being examined;

deriving a set of weighted crystallographic phases by assigning a low weighting factor to the crystallographic phases of the model crystal structure;

using the set of weighted crystallographic phases and combining with the observed structure factor amplitudes to derive the ~~first~~ electron density map; and

combining the set of weighted crystallographic phases with the crystallographic phase probability distributions from claim 1 step (g) to form a composite set of crystallographic phase probability distributions.